REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims are 1 to 10 are in the case.

CLAIM REJECTIONS – 35 USC s. 103

The Examiner has rejected claims 1 to 10 as allegedly unpatentable over Mordehai et al. (U.S. patent No. 5,672,868), in view of Takada et al. (U.S. patent No. 5,481,107). This rejection is respectfully traversed, and it is respectfully submitted that the present invention as claimed is patentable over the combined teachings of Mordehai et al. and Takada et al. Before addressing the argument in detail, the invention and its relationship to the known art is summarized.

BACKGROUND AND SUMMARY OF INVENTION

The present invention relates to a method and device for preventing ion source gases from entering reaction/collision cells in mass spectrometry. Typically, a reaction/collision cell is maintained at a pressure between $5x10^{-3}$ Torr to $5x10^{-2}$ Torr when reaction or collision induced disassociation is required. This pressure is provided by a reaction/collision gas.

Upstream of the reaction/collision chamber, a sample is fed into a plasma that is maintained in an excited or energized state by inductive coupling. The plasma typically includes the analyte, usually a metal and usually ionized, and various other constituents, such as argon, oxygen, hydrogen and water vapor, most of which will commonly be neutral but some of which (about 0.1% of the Ar, for example) may be ionized. For wet plasma, which is typically used, the content of reactive neutrals, such as hydrogen, oxygen and their various polyatomic combinations, is as high as 17%. The (typically) atmospheric pressure plasma, including these ions and neutrals, expands into a chamber maintained at approximately 4 Torr. From this chamber, the plasma on source stream passes through a skimmer into a chamber maintained at a low pressure of 10^{-3} Torr. From this chamber, the ions then are intended to pass into the reaction/collision cell, maintained at a higher pressure of, e.g., 5×10^{-3} to 10^{-2} Torr.

Before analyzing the behaviour of the various constituents of an ion source stream, it must first be understood that, in accordance with the law of conservation of energy, kinetic energy and pressure are interchangeable, i.e., when the ion source stream passes from a high pressure to a low pressure, it accelerates and individual ions and neutrals gain velocity. Conversely, when passing from a region of low pressure to a region of high pressure, the (at least neutral portion of the) flow decelerates; this is

sometimes expressed as an "impact pressure", since the deceleration of a flow creates a pressure differential, the impact pressure.

A simple analysis suggests that the higher pressure within the reaction/collision cell (i.e. higher than the stagnation pressure of the preceding chamber) would prevent neutral species from the ion source stream from passing into the reaction/collision cell. Indeed, because of the higher pressure within the collision/reaction cell, there is always a flow of the reaction/collision gas out of the cell against the ion flow. Accordingly, only ions driven by the potential gradients of electrostatic focusing fields will overcome the higher pressure to pass into the reaction/collision cell. However, this simple analysis overlooks any "impact velocity" that the ions and neutrals might have.

The present invention is based on an important realization by the inventors, not previously recognized in this art, that an ion source stream flowing into a collision cell may have a significant impact pressure. This occurs because the ion source stream expands supersonically from the atmospheric pressure source through the sampler into the approximately 4 Torr region and thence through the skimmer into the chamber at 10^{-3} Torr. As is known, the purpose of this chamber at the low pressure of 10^{-3} Torr, is to enhance extraction and removal of unwanted neutrals so as to enhance the ratio of ions to neutrals passing on to further processing. What the inventors have realized is that there are too few collisions with the background gas in the low pressure (10^{-3} Torr) chamber to disrupt the directed flow and convert this to random (thermal) flow. Hence, when these ions and neutrals reach the inlet of the reaction/collision cell, they can generate an impact pressure sufficient to overcome the pressure differential (at most a multiple of 10^{-2} Torr) at the entrance of the collision cell. Consequently, individual ions and neutrals within the supersonic expansion jet, after passing through the skimmer into the regions at 10^{-3} Torr, may have sufficient momentum to overcome the pressure differential between the higher pressure in the reaction/collision cell and the lower pressure of the region at 10^{-3} Torr, thereby passing into the reaction/collision cell.

Ion-molecule reaction/collision cells are widely used in inductively coupled mass spectrometry (ICP-MS). The successful operation of these cells depends on how pure the reaction gas is. If neutral gas particles from the ion source stream are entrained into the flow into the reaction/collision cell, then the reactions within the reaction/collision cell will not be controlled anymore. Instead of the high purity reaction gas introduced intentionally to the cell, a mixture of the reaction gas with entrained ion source streamgases is instead introduced. These plasma gases may be up to 17% composed of reactive neutrals, such as hydrogen, oxygen and various polyatomic combinations of hydrogen and oxygen. Despite the fact that the pressure in the pressurized cell may be higher than the background pressure of the vacuum compartment where the cell is positioned, the gases from the ion source stream can still enter the cell because, as

noted above, the ion source streamgas undergoes supersonic expansion in the plasma-vacuum interface, after which particles travel with a terminal speed of about 2300 m/second typically. The impact pressure of such high velocity gas particles can be sufficiently higher than the pressure of the reaction/collision cell in the gas, so that the neutral gas particles from the ion source stream will be entrained into the reaction/collision cell.

The claims of the application are directed to mass spectrometer systems and methods of operating mass spectrometer systems that overcome or mitigate the above-described problems. Claim 1 covers mass spectrometers that include an ion source, an ion interface, a reaction/collision cell section for receiving the ions from the ion interface, and an ion-neutral decoupling device provided between the ion interface and the reaction/collision cell section, to provide substantial separation between ions and neutral particles. The ion interface provides an interface to the ions between the ion source and the reaction/collision cell section. Thus, the ion-neutral decoupling device provides substantial separation between ions and neutral particles before the neutral particles contaminate the gas within the reaction/collision cell.

Similarly, claim 6, the independent method claim, covers a method of operating a mass spectrometer system. The method comprises (i) supplying a sample to an ion source and generating an ion source stream, including sample ions and unwanted neutral particles; (ii) separating neutral particles from the ion stream; and then (iii) passing the ion stream into a reaction/collision cell section. Thus, the method stipulates that the neutral particles be separated from the ion stream before the ion stream is passed into the reaction/collision cell section

AMENDMENTS TO THE SPECIFICATION AND CLAIMS

In the specification, the Summary of the Invention section has been amended to bring the two statements of invention into agreement with the amended claims. Additionally, the term "reaction/collision cell section" has been defined, to ensure that this term is definite.

In order to clarify the nature of the stream originating from the ion source, this is now labeled in claims 1 and 6 as am "ion source stream". Corresponding to this amendment to claims 1 and 6, page 9, lines 10 and 13 is being amended to refer to ion source stream, and the first entry also includes a reference to the term "plasma". The specification at numerous places refers to the ion stream in different ways, and indicates that this can be labeled as a "plasma"; note in particular the passage at page 1, lines 22 – 25. Thus, no new matter has been added. This amendment is merely

intended to make it clear that the stream of particles from the ion source comprises both ions and neutrals.

Additionally, to ensure that there is a clear antecedent for the reference to neutrals, this term is now introduced in the paragraph describing the ion source in claim 1. Again, no new matter has been added.

Dealing with other amendments, a minor typographical error has been corrected in the last line of the paragraph bridging pages 8 and 9. The paragraph bridging pages 9 and 10 has been amended, similar to the amendment to the Summary of the Invention section, to clarify the function of the reaction collision cell. Minor typographical errors are being corrected in the paragraph on page 11. None of these amendments comprise new matter.

Claim 1 has first been amended so that it now claims a "mass spectrometer system" rather than simply a "mass spectrometer". This is for two reasons. Firstly, it ensures consistency with claims 2-5. Secondly, it is intended to emphasize that the mass spectrometer system does not necessarily include a mass analysis step. In its broadest concept, the present invention is concerned with decoupling of ions and neutrals upstream from a reaction/collision cell, and what further processing is applied to the ions, downstream from the cell, is not critical to the invention.

Claim 1 has been further amended to specify that the reaction/collision cell section is "for processing the ions received from the ion interface". The intention here is to make it clear that the reaction/collision cell provides for "processing" of the ions, but not necessarily for mass analysis. Indeed, reaction/collision cells are inherently ill suited for mass analysis due to the relatively high pressures therein, and it is common to carry out mass analysis in a separate, downstream mass analysis section. As noted above, whether or not such mass analysis is effected is not essential to the present invention.

It is here emphasized that the present invention is directed to separation of ions and neutrals immediately upstream of or before a reaction/collision cell. As explained, it has previously been thought that, due to the high pressure of a reaction/collision cell, there should be little problem with neutrals entering such a cell. However, the present inventors have now realized that an ion stream, and particularly neutrals in such a stream, can have a sufficiently high impact pressure to enter such a cell.

The final phrase of claim 1 has been deleted. It is noted that the end of claim 1 now requires the decoupling device to provide "substantial separation" between ions and neutral particles, which is the correct way to define such separation, as separation can never be perfect. The deleted phrase was inconsistent with this reference to substantial

separation, and hence, to ensure that the claim is definite, this phrase has been deleted.

Claim 6 has been amended, somewhat correspondingly to the amendments to claim 1. Thus, the reference to "mass analysis" has now been removed from claim 6, since the three steps set out in claim 6 do not, in fact, provide for mass analysis. Step 3 of claim 6 has been amended to delete the reference to analysis. This adds no new matter and is entirely consistent with the application as originally filed. As is well known, collision/reaction cells are used mainly to cause fragmentation or reaction of ions, for further processing. Analysis of any sort is not carried out in conventional reaction/collision cells. It is believed that this original wording of claim 6 may have caused some misunderstanding, and as explained below, it is submitted that claim 6, as amended, is now clearly distinguished from the cited art.

In claim 9, the last two lines have been revised as shown, simply to clarify the claim and render the claim more definite. The reference to "kinetic energy" has been removed, since it does not appear to add anything to the claim. Again, the point is that by providing an obstruction to the neutral particles, then any "impact pressure resulting from conversion of kinetic energy to pressure" cannot be achieved, so that the neutral particles will not tend to pass into the collision cell.

In claim 10, reflecting the fact that claim 6 now clearly no longer claims mass analysis, the wording has been amended to state that step (3) comprises passing the ions in the collision/reaction cell, and that the ions are then subject to mass analysis, this being introduced for the first time in claim 10.

All amendments to the claims have been made for reasons unrelated to patentability

It is here noted that the abstract is being amended corresponding to the amendment to claim 1.

DETAILED REPLY TO CLAIM REJECTIONS

Mordehai et al. provides an example of the above-described problem that the present invention is intended to overcome or mitigate. That is, in the Mordehai configuration, the ion source is aligned with the entrance of an RF ion guide such that the high velocity of the neutral particles from the ion source provide an impact pressure at the entrance to the RF ion guide that is sufficiently higher than the pressures in the range of 10^{-1} to 10^{-4} Torr within the reaction/collision cell in the gas, such that the neutral particles are entrained into the reaction/collision cell.

Referring to Figures 1 and 6 of Mordehai et al., there is illustrated, in schematic drawings, a mass spectrometer using a tilted capillary. Ions leave the capillary and are transferred to the pressurized RF ion guide. The two dashed lines shown in these figures designate the axes of the capillary transfer tube and the RF ion guide. As can clearly be seen from Figures 1 and 6, the axis 6 of the capillary transfer tube intersects directly into the opening into the RF ion guide. This indicates that the source neutrals can enter the RF ion guide (provided, of course, that the impact pressure of the source neutrals exceeds the RF ion guide – note that region 8, just in front of the RF ion guide, designates a region of an aerodynamic jet, which implies that the impact pressure will be comparatively high).

Accordingly, it is respectfully submitted that Mordehai fails to disclose separation before the ion guide and just discloses separation of the source neutrals and the ions within the RF ion guide. In contrast, the present invention provides for separation of the source neutrals and ions before, or at the entrance of, the collision/reaction cell, to prevent ingress of the source neutrals into the cell. Note the passage of Column 5, lines 36-40, where Mordehai specifically teaches positioning the rods of the RF guide 16, to avoid collision with the neutrals, thus permitting the neutrals to pass between them and out of the guide.

Mordehai thus allows source neutrals to enter into the pressurized RF ion guide. The source neutrals are then to be ejected from the RF ion guide without colliding with the individual rods of the guide, into the intermediate region 4a. The source neutrals can then be pumped out of region 4a. However, what Mordehai fails to realize is that while the neutrals are within the RF ion guide, these source neutrals may participate in unwanted ion-molecule reactions.. Indeed, Mordehai et al. provides no reason or basis for preventing the introduction of both ions and neutrals into the RF ion guide, as there is no mention in Mordehai et al. that the ions may react with the source neutrals inside the RF ion guide, or that the source neutrals that are entrained into the RF ion guide (collision/reaction cell) may contaminate the cell pressurizing gas. That Mordehai et al. does not teach impeding source neutrals from entering the RF ion guide can be seen not only from Figures 1 and 6, but also from column 8, line 64 to column 9, line 2 where it is clearly stated that the direction of ion motion and direction of neutrals are differentiated due to the action of the RF quadrupole ion guide. In other words, it is the RF ion guide that separates the ions and neutrals. In order to achieve this, the ions and neutrals must be introduced into the RF ion guide together. Then the action of the RF ion guide (collisions with the pressurizing gas molecules and the effect of the RF fields) is intended to provide separation between the ions and neutrals. As noted, this approach is problematic, and the present invention is intended to avoid it, by impeding incursion of the source neutrals into the cell.

The Examiner, in paragraph 3 of the action, referred to various passages of Mordehai. These are hard to understand. Firstly, it is noted that the Examiner seems to have, somewhat arbitrarily, picked out various passages from Mordehai that refer to different embodiments of Mordehai, and assumed that these can be somehow pieced together to form a whole.

Thus, column 4, lines 40-41 and column 7, lines 9-10, both cited for showing an ion source, refer, separately, to figures 1 and 7. The passage at column 4, line 34 is cited for showing an ion interface, but this merely refers to a "radio frequency ion guide", in figures 9a and 9b. Then, the Examiner cites the passage at column 6, line 56 (the figure 6 embodiment), which notes that an RF guide can be pressurized. He also refers to the passage here, and passages at column 6, line 62-64 and column 7, lines 15-16 for showing reaction/collision of the molecules involved. In fact, the passage at column 7, lines 15-16 refers not to the gas used to pressurize the RF ion guide, but to a heated "curtain gas", which helps to decluster the source ions before they are sampled into the RF ion guide. This is a known technique in this art, and entirely separate from the issue of reaction/collision.

A passage at the foot of column 4 and column 5, lines 6-8 is cited for showing a mass analyzer. In fact, the passage cited at column 5 refers to a collisional region in front of the RF ion guide.

The passage at column 2, lines 54-57 was cited by the Examiner for showing an electrostatic lens for deflecting ions. This passage is in the background for the invention section, and refers to the Takada '107 patent. If this whole paragraph is taken, i.e., column 2, lines 53-63, it is clear that Mordehai is teaching directly away from the Takada et al. proposal. It is noted that the Takada et al. teaching "being an advanced one has a drawback in certain respects. The electrostatic lens in this design is positioned in the relatively high pressure vacuum region. It is a well know fact that electrostatic optics under high vacuum pressure cannot provide an efficient ion focusing due to intensive ion scattering, which leads to ion loss and reduced ion transmission".

Thus, Mordehai makes it quite clear that the intention is to provide an alternative to the Takada et al. proposal.

The Examiner then argues that Mordehai shows decoupling ions and neutrals between an ion interface and the reaction/collision region, and refers to an area close to items 8 and 12 in figures 1 and 6.

If one takes the Examiner's analysis, i.e., that Mordehai primarily teaches a reaction or collision somewhere close to the items 8 and 12, then this teaches directly away from

the present invention. In effect, what Mordehai is teaching is that when one allows the reaction/collision to take place, and then, somewhere downstream, at the entrance to the RF ion guide 16, the neutrals are separated from the ions. By this point, the presence of unwanted neutrals has already degraded the reaction/collision processes. In contrast, the present invention is intended to achieve as efficient separation of ions and neutrals as possible, upstream of the collision/reaction location.

With respect to claim 9, this is directed to the feature of providing an ion stream that passes through an aperture into a substantially sub-atmospheric pressure, thereby generating an expanding supersonic jet, i.e., with the ion optics compartment between the ion source and the collision/reaction cell. It is the unique pressure characteristics resulting from such an ion optics compartment, which causes the problem addressed by the present invention. Thus, the pressure drops significantly at the inlet to the compartment, accelerating the ions, and then rises again as the ion stream passes into the collision cell. To reiterate, what the present inventors have realized is that the substantial, initial pressure drop into the compartment accelerates the ions and neutrals, in the supersonic jet, and these particles can then maintain their kinetic energy sufficiently to enable them to enter the reaction/collision cell.

The Examiner identified the aperture as item 12 in figures 1 and 6 and the volume maintained at sub-atmospheric pressure was identified by the Examiner as the region 4a, containing the ion guide 16, based on the Examiner's reference to column 6, lines 50-52 and 60-62. The Examiner then referred to column 4, line 54 and column 7, lines 23 and lines 39-40 for showing an aerodynamic jet. The passage at column 4 makes no reference to an aerodynamic jet. Column 7 refers to figure 7, an entirely different configuration which does make reference to an aerodynamic jet at line 23. The passage at lines 39-40 of column 7 refers to yet another figure, concerned with use of gas chromatography. None of these arrangements provide, in series, an aperture opening into an ion optic compartment for generating an expanding supersonic jet, the ion optics compartment, and downstream from the ion optics compartment a separate and distinct collision/reaction cell.

The Examiner referred to column 8, lines 48-49 for the step of separating neutral particles from ions. This sentence merely indicates that the system for transporting and separating ions may be useful for other purposes. The Examiner further referred column 7, lines 6-7 for obstruction or a restriction to the particles. This passage refers to a conical skimmer 18, which is entirely conventional. Providing conical skimmers and the like to maintain pressure differences between different compartments and to keep loads on pumps reasonable is well known within the mass spectrometer art. Conventionally, such skimmers have relatively small apertures, to maintain these pressure references and to enable pumps of reasonable size to be provided. The passage cited by the

Examiner refers to the conical skimmer as acting as a "restriction" i.e., in an entirely conventional manner, and there is not suggestion that this be positioned to act in any sort of "obstruction" manner.

Again, the Examiner's analysis of Mordehai et al. appears to rely upon a complex, hybrid structure developed by using hindsight to pick and choose from the various elements disclosed in the different embodiments of Mordehai et al. Such a hybrid structure is nowhere specifically taught or suggested in the '868 patent itself.

What is clear in Mordehai et al. and what is common in all the proposals is that separation of ions and neutrals takes place in the ion guide 16 itself. Where the RF ion guide operates as a collision cell, collisions with the gas in the cell cause the ion energies to be quenched, which allows the ions to be focused through the RF ion guide in known manner while the neutrals are unaffected by the RF field. Clearly, separation takes within the ion guide.

Mordehai et al. fails to mention that the ions may react with the source neutrals inside the RF ion guide where the source neutrals that are entrained in the RF ion guide could serve as contaminants of the cells pressurizing gas. Again, there is no mention that, with relatively high pressure present, the neutrals will not simply pass at an angle out of the RF ion guide, but may well enter into various collisions so as to be retained within the RF ion guide. Mordehai et al. failed to mention that such reactions may be unwanted, so as to decrease to signals of the desired ions and/or create new interfering ions.

For all these reasons, Mordehai et al. failed to realize that there is any necessity or desirability to separate the ions and neutrals before entry of the ion into a reaction/collision cell, as taught by the present invention.

In column 7, lines 6-7: while it might be that the conical skimmer (item 18 of figure 7) serves as a restriction to some of the neutral flow, it does not disrupt the directed flow of the neutral species that are transmitted through it. In fact, the conical skimmer serves much the same function as any skimmer (even as used in the ICP-MS and to which the present application refers); it skims the beam. A proper skimmer does not substantially distort the directed flow of the gas that it skims. Rather, figure 7 indicated that source neutrals and ions are transmitted through coaxial sampling nozzle (item 17) and conical skimmer (item 18) through to the RF ion guide (item 16). Hence, the directed flow of the expanding source gases is directed at the entrance of the RF ion guide. A means to disrupt the directed flow of the gas so as to minimize incursion of the source neutrals into the RF ion guide is nowhere suggested or provided.

Column 9, lines 1-2: this section is a final, summary paragraph, and the cited passage is largely a claimed benefit of the invention. It also appears that it should be read with the preceding section in column 8, lines 64-67, in which it is clearly stated that the direction of ion motion and direction of neutrals are differentiated due to the action of the radio-frequency quadrupole ion guide. This is the important issue. Throughout this patent, it is taught that it is the RF ion guide that separates the ions and neutrals. In order to achieve this, the ions and neutrals are introduced into the RF ion guide together, and the action of the RF ion guide (collisions with the pressurizing gas molecules and the effect of the RF fields) is intended to separate the ions and neutrals. It must be understood that when the source neutrals are introduced into the RF ion guide, they necessarily contaminate the gas contained within the RF ion guide. If the ions react with the source has, then such reactions will be promoted within the RF ion guide. This is what the present invention precludes, by separating the ions and neutrals before the entrance of the RF ion guide (or collision cell). Note also the subsequent passage (column 9, lines 2-5) that clearly indicates that the ions are separated from the neutrals by the action of electrical fields (not by physical disruption of the beam, as in the present invention); Mordehai is saying that the ions are focused through the RF ion guide (particularly after they are collisionally quenched) because of the action of the RF field, which has no effect on the motion of the neutral species. It is not recognized that collisions of the ions with the source neutrals can result in unwanted ion-molecule reactions, and hence Mordehai saw no reason to attempt to separate the ions from the neutrals before the entrance of the RF ion guide.

With respect to claims 1, 6, 2-3 and 8, the Examiner correctly noted the Mordehai et al. failed to disclose an ion/neutral decoupling device comprising of a or a plurality of plates with offset apertures with respect to one another, so as to prevent direct passage of neutral particles, as defined in claim 2 of the present invention. The Examiner then went on to argue that Takada et al. disclosed the necessary offset apertures. This rejection is respectfully traversed.

Takada et al. teach that ions can be separated from neutrals by applying electrostatic fields that bend the ion beam from one axis (the source sampling axis) to another axis (the mass analyzer axis) in such a way that the neutral species are not focused into the mass analyzer device. However, Takada et al. do not teach the use of a collision cell or reaction cell, or that contamination of the gas contained within such a cell by neutrals obtained from the source may promote unwanted ion-molecule reactions. Hence, Takada in no way suggests the need for any device or method for separating the source ions from the source neutrals before the ions are introduced into a collision cell or reaction cell. Furthermore, since Mordehai et al. do not recognize the negative results from introducing source neutrals into a collision cell or a reaction cell (which lack of recognition can be seen from the fact that Mordehai et al. teaches introducing both

source neutrals and ions into the collision/reaction cell), the combined teachings of Takada et al. and Mordehai et al. do not render the present invention obvious.

Takada et al. is also noteworthy for being distinct from the present invention for a number of reasons. Firstly, Takada et al. is primarily concerned with mass analysis of organic compounds and the like. For example, column 1, lines 8 and 9 indicates that it is concerned with a spectrometer for separate analysis of "human body relating mixture compounds such as saccharides, peptides, proteins, and so on". Mass spectrometers are certainly well known for such analysis, and form a distinct group or class of mass spectrometers. Analyzing such organic compounds requires careful handling of the compounds, since the compounds are usually relatively large, organic molecules which are quite delicate. In particular, subjecting such compounds to extreme temperatures and the like rapidly degrades the sample and results in breakup of the sample molecules. In contrast, the present invention is primarily concerned with analysis of inorganic compounds; such inorganic compounds are commonly analyzed by inductively coupled mass spectrometry (ICP/MS). Here, to generate an ionized sample, an argon plasma is used. In such a plasma, very high temperatures are present, and this is entirely unsuited for use with organic molecules.

Accordingly, a person skilled in ICP/MS would not, routinely, consider the art of mass spectrometry for organic analysis

It is also to be noted that Takada et al. provide the electrostatic lens 21 before a mass analysis region 6, including a quadrupole rod set. This is clearly intended to select an ion for analysis which is detected by an ion detector 8. Thus, nowhere does Takada et al. suggest the use of a collision cell, so that the whole problem of unwanted neutrals entering a collision cell is nowhere recognized or addressed in Takada et al. As mentioned, conventional thinking has been that due to the high pressure in collision cells and the fact that there is always a flow of the collision/reaction gas out from the cell and against the ion stream flow, then this must surely prevent or significantly impede passage of unwanted neutrals into the collision/reaction cell. Thus, based on this conventional thinking, there is no reason or basis to consider adoption of any such arrangement as taught by Takada et al. Rather, a skilled person would be reluctant to use the configuration of Takada et al., since it might well result in loss of part of the ion signal.

Accordingly, it is again submitted that a key aspect of the present invention is not just the detailed implementation of the invention, but firstly recognizing and addressing the unique problem of unwanted contamination of collision cells. This problem has nowhere been recognized in the art, and conventional thinking has been that there should be no problem, due to the inherent high pressure within a collision/reaction cell. This is borne

out by the fact that most instruments described in the known literature, prior to the present invention, were configured to expose the collision/reaction cell directly to the unimpeded flow of the source gas. Such configurations can be readily found in commercially available instruments.

With respect to the passage at column 3, lines 25 and 26, this does not refer to offset apertures, but rather to two coaxial cylindrical electrodes, one inside the other, where holes are provided in the inner cylinder to allow the potential applied to the outer cylinder to penetrate through the inner cylinder. The ions do not pass through these holes and they are not aperture lenses.

Accordingly, the Examiner's rejection of claims 1, 6, 2-3 and 8 as being obvious is respectfully traversed.

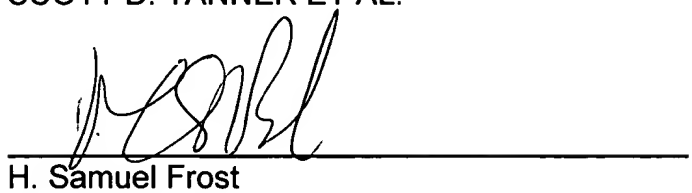
The Examiner also cited Okamoto (U.S. patent No. 5,049,739), but did not specifically rely upon this reference. It is respectfully submitted that Okamoto is not relevant to the present invention. Specifically, Okamoto does not refer to discrimination against neutral species obtained from a plasma source, but rather to neutral species that are products of charge exchange reactions of plasma ions, where these reactions occur within the reaction chamber. Further, discrimination against these neutral species that are formed in the reaction chamber is obtained by electrostatic means downstream of the reaction chamber. Most significantly, the configuration of Okamoto (shown in Figure 3) indicates that the reaction chamber is aligned with a sampling axis (see also column 3, lines 28 to 29, which notes that the energy analyzer is aligned with the axis of the injected beam, which, in turn, implies that the optical elements in the reaction chamber are aligned with the axis of the injected beam). No means is provided to disrupt the flow of the source neutrals, with the result that these source neutrals may enter the reaction chamber (depending on the impact pressure in the reaction chamber pressure at the entrance of the reaction chamber). Accordingly, Okamoto does not teach the separation of the source ions and neutrals before the reaction chamber.

In view of the foregoing, it is respectfully submitted that the claims are allowable over the cited references. Allowance of the application is respectfully requested.

If any questions arise, it is requested that the undersigned be contacted at the number provided below.

Respectfully submitted,

SCOTT D. TANNER ET AL.



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please replace the Summary of the Invention from page 7, line 32 to page 8, line 17, with the following:

In accordance with a first aspect of the present invention, there is provided a mass spectrometer system comprising:

an ion source for producing an ion source stream comprising sample ions and neutrals;

an ion interface;

a reaction/collision cell section for processing the ions received from the ion interface, with the ion interface providing an interface ~~to the~~ ions for the ion source stream between the ion source and the reaction/collision cell section; and

an ion-neutral decoupling device provided between the ion interface and the reaction/collision cell section, to provide substantial separation between ions and neutral particles ~~whereby only ions pass on to the reaction/collision cell section.~~.

As used in the specification including the claims, the term "reaction/collision cell section" is a cell operated at a suitable pressure to effect at least one of collision and reaction, as required.

In accordance with another aspect of the present invention, there is provided a method of operating a mass spectrometer system, in which ions are generated and ~~subject to mass analysis~~ processed, the method comprising:

(i) supplying a sample to an ion source and generating ~~a~~ an ion source stream of ions, including sample ions and unwanted neutral particles;

(ii) separating neutral particles from ~~the~~ an ion stream; and then

(iii) passing the ion stream into a reaction/collision cell section ~~for analysis~~.

Please amend the three paragraphs from page 8, line 32 to page 9, line 22 as follows:

Reference will first be made to Figure 1, which shows a mass spectrometer indicated generally by the reference 10. The mass spectrometer 10 includes a sample introduction system 12, that can be any known and suitable sample introduction system. The sample introduction system 12 is connected to an ion source 14. Any suitable, known sample introduction system 12 and ion source 14 can be used. For example, these two elements 12, 14 can comprise an electro spray source, for generating ions from a sample analyte desolved in solution. A nebulizer / spray chamber / ICP is another example of an arrangement of the sample introduction system 12 and the ion source 14. However, any suitable sample introduction system and ion source can be used.

Figure 1 inherently assumes that the ion source 14 is at higher pressure than the ion optics compartment 18. ~~Ions~~ An ion source stream or plasma from the ion source 14 passes to a differential pumping interface 16. Commonly, for an atmospheric pressure source, this would be an intermediate pressure chamber operating at around 4 Torr.

From the pumping interface 16, ~~ions are passed~~ the ion source stream passes into a compartment identified as an ion optics compartment 18. This will be maintained at a low pressure, typically 10^{-3} Torr. The wall 20 separating the ion optics compartment 18 from the differential pumping interface 16 can comprise a skimmer cone or the like. As described above, the pressure difference between the ion source 14 and differential pumping interface 16 creates a high velocity supersonic jet, indicated at 22, that enters the ion optics compartment 18. This supersonic jet would have the composition outlined above, i.e. typically sample particles, argon atoms largely neutral, and significant amounts of, for example, oxygen, hydrogen and their different polyatomic combinations, largely neutral.

Please amend the paragraph from page 9, line 31 to page 10, line 6, as follows:

A reaction cell or collision device or cell 30 is provided. This reaction in collision cell is operated to effect at least one of reaction and collision and fragmentation, as required. As detailed above, this operates at a different pressure range, typically either in a range of 10^{-3} Torr – 10^{-2} Torr with a reaction gas present, or the low pressure of 10^{-5} Torr when no reaction is to take place. It is shown having one end forming an interface with the ion optics compartment and the other end outside of the ion optics compartment 18. For some applications, the reaction or collision cell device 30 could be located wholly within the ion optics compartment 18, so that the ion stream is subjected to the pressure of the ion optics compartment 18 both before and after passing through the collision device 30 .

Please amend the paragraph on page 11, lines 14 – 21 as follows:

It is here noted that, in a known manner, the different sections of the whole mass spectrometer apparatus or device would be provided with appropriate pumps to maintain the desired pressure. Additionally, these pumps, in known manner, can be cascaded. For example, a roughing pump maintaining a pressure of the order of a few Torr can also be used to backup a higher performance pump maintaining pressures of the order of mTorr or lower in the ions optics compartment. ~~Ast~~ 49 in Figure 2, and also Figures 3-9, there is shown an opening for connection to such a pump.

IN THE CLAIMS

Claims 1, 6, 9 and 10 have been amended as follows:

1. (Amended) A mass spectrometer system comprising:

an ion source for producing an ion source stream comprising sample ions and neutrals;

an ion interface;

a reaction/collision cell section for processing the ions received from the ion interface, with the ion interface providing an interface for the ion source stream between the ion source and the reaction/collision cell section; and

an ion-neutral decoupling device provided between the ion interface and the reaction/collision cell section, to provide substantial separation between ions and neutral particles~~, whereby only ions pass on the reaction/collision cell section~~.

6. (Amended) A method of operating a mass spectrometer system, in which ions are generated and ~~subject to mass analysis~~ processed, the method comprising:

(i) supplying a sample to an ion source and generating an ion source stream, including sample ions and unwanted neutral particles;

(ii) separating neutral particles from an ~~the~~ ion stream; and then

(iii) passing the ion stream into a reaction/collision cell section ~~for analysis~~.

9. (Amended) A method as claimed in claim 6, which includes generating the ion source stream at atmospheric pressure, passing the ion source stream through an aperture into an ion optics compartment maintained at a substantially sub-atmospheric pressure, thereby to generate an expanding supersonic jet, wherein step (ii) includes obstructiong the supersonic jet, ~~thereby~~ to ~~prevent the kinetic energy of the jet promoting~~ obstruct passage of neutral particles into the reaction/collision cell section.

10. (Amended) A method as claimed in claim 6 wherein step (iii) comprises ~~the mass analysis step includes~~ passing the ions into ~~a~~ the collision/reaction cell section for collision and/or reaction, and subsequently subjecting the ions to mass analysis.

IN THE ABSTRACT

A mass spectrometer has an ion source for producing sample ions. The ions pass through an ion interface, to a reaction/collision cell section. An ion-neutral

decoupling device is provided between the ion interface and the reaction/collision cell section, to provide substantial separation between ions and neutral particles~~, whereby only ions pass on to the reaction/collision cell section~~. The supersonic jet entering the spectrometer can have sufficient energy to cause the plasma gases, such as argon, to overcome the pressure differential between the reaction/collision cell and an upstream section of the spectrometer so as to penetrate into the reaction/collision cell; the decoupling device prevents this. The decoupling device can have offset apertures provided by plates or rods or other comparable arrangements, or can comprise a quadrupolar electrostatic deflector, an electrostatic sector deflector or a magnetic sector deflector.